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Discussion

Dr Richard Weisel *(Toronto, Ontario, Canada).* Thank you very much for an excellent presentation and congratulations to your group for a very difficult study in these large animal models. This study represents a real tour de force. The proposal to enhance mesenchymal stem cell (MSC) engraftment is very important. Another approach is to use the hydrogels that were described earlier to improve cell survival. Another alternative is to reduce the inflammatory phase, as Dr Mayer discussed earlier, which is a very important concept. Of course this is what MSCs do normally. The implantation of MSCs into the heart induces the proliferation of T regulatory cells (Tregs), 1 of the major beneficial effects of MSC treatment. Therefore, the transplantation of Tregs with MSCs is enhancing the endogenous repair mechanisms that result from MSC therapy. This approach is a great idea.

Did you actually improve MSC survival? Was the number of MSCs in the heart greater with the Tregs?

Dr Zhou. These are good questions. It is difficult to quantitatively count the total number of these cells at 6 weeks after injection to see if they increased. However, evidence of an increase includes the very dense and sphere-shaped clusters surrounded by thin, layered capsules seen on serial tissue section analysis. These were never found in the MSC-only injection heart. We believe the cell number was increased compared with MSC only, but it's difficult to give a quantitative answer to this question.

Dr Weisel. Did you improve heart function?

Dr Zhou. This is preliminary data and this project is still ongoing. We are testing the functional improvement by performing stress echo and magnetic resonance imaging before and after cell transplantation. The data will be shown in the near future.

Dr Weisel. The cotransplantation of Tregs and MSC was beneficial for autologous cell therapy but may be very important for allogeneic cell therapy. As you know, many investigators are now proposing allogeneic rather than autologous cell therapy because of the tremendous opportunity to have an off-the-shelf product for patients who need it, particularly in the operating room. Have you tried this approach for allogeneic cells? Cotransplantation of Tregs and MSCs would be much more relevant for allogeneic cell therapy.

Dr Zhou. We tried allogeneic cell therapy using green fluorescent cells and published those results previously. But during that study we did not involve Tregs. I think it is an excellent idea to do it in the future.